



Medical microbiology

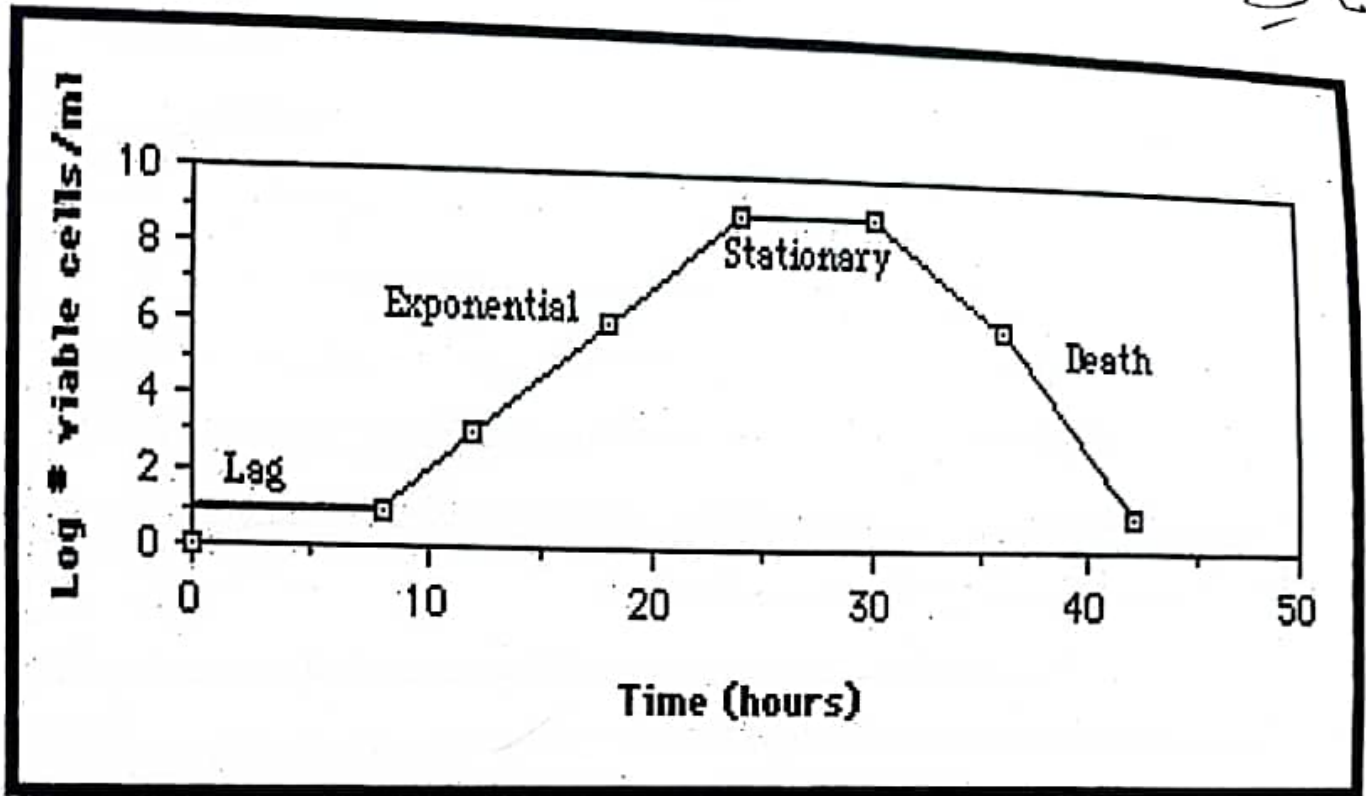
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The first stage

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اطلسبب الامراض
Pathogenicity

احياء نظري
اول علم طبي
فصل ثاني



مقدرة
Infection: The few microbial species that are able to invade and then damage tissue and cause disease are called pathogenic infection. The capacity of a microorganism to cause disease is referred to as pathogenicity.

بعض
Some microorganisms cause a single characteristic disease, e.g. *Clostridium tetani*, which causes tetanus. Other microorganisms can cause a wide range of different diseases. For example, *Staphylococcus aureus* can cause skin infections such as abscesses and wound infection, pneumonia and osteomyelitis, other microorganisms are able to cause disease only in individuals with impaired defenses and are called opportunistic pathogens.

Virulence

The term virulence is used to describe the degree of pathogenicity a microorganism to cause disease. Virulence depends on the microorganisms' ability to invade, multiply in and damage the host and is mediated by factors in both the host and the microorganism. The ability of a microbe cause disease depends on some factors that:

- 1- Assist adhesion (e.g. fimbriae, slime).
- 2- extracellular enzymes (e.g. Urease ,protease , Hemolysin).
- 3- Protect against the immune system (e.g. capsules).
4. Determine toxin production.

Methods of Transmission of Infection

- 1- Contact: gonorrhoea, trachoma.
- 2- Inhalation: Influenza, tuberculosis.
- 3- Infection: Cholera (water) food poisoning (food dysentery).
- 4- inoculation organism : rabies (dog)
- 5- Insects: Act as mechanical vector (dysentery and typhoid by house fly) or biological vector (malaria) of infection disease.
- 6- Genital: syphilis, Trichomonas.
- 7- Laboratory infection: Infection may be transmitted during procedure like injection.

Bacterial toxins

Toxins: are substances released by microbial cells, which by damaging or destroying specific tissues are responsible for some or all of the disease processes. **There are two types of toxin.**

- 1- **Exotoxins** are usually protein enzymes secreted by bacteria into their local environment. They may be transported in the bloodstream and cause damage in parts of the body remote from the site of infection..
- 2- **Endotoxins:** are lipopolysaccharides contained in the outer cell membrane of Gram -negative bacteria. They do not have enzymatic activity but have profound systemic effects on the host, including:
 - 1- Induction of high fever.
 - 2- Reduction in blood pressure and disruption in coagulation causing bleeding into the tissues.

Stages in the Development of Infection

- 1- Acquisition
- 2- Adhesion to host cells Penetration of cells.
- 3- Damage to tissues
- 4- Spread to other tissue
- 5- Resolution or death

Source of Infection

- 1- Man is himself a common source of infection from a patient or carrier. Healthy carrier is a person harboring pathogenic organism without causing any disease to him.
- 2- Animals: Infection diseases transmitted from animals to man. Zoonosis may be bacteria (e.g. rickettsia).
- 3- Insects: The disease caused by insect are called arthropod borne disease. Insects like mosquitoes, lice that transmit infection are called vector.
- 4- Some vector may act as reservoir host (e.g. ticks in spotted fever).
- 5- Soil: Soil may serve as some of parasiting infection like round worm and hook worm. Spore of tetanus bacilli remain viable in soil for a long time.
- 6- Water: Cholera vibrio, infective hepatitis virus, guinea worm may be found in water.
- 7- Food: Contaminated food may be a source of infection. Presence of pathogens in food may be due to external contamination (e.g. food poisoning by staphylococcus).

Bacterial Growth Curve

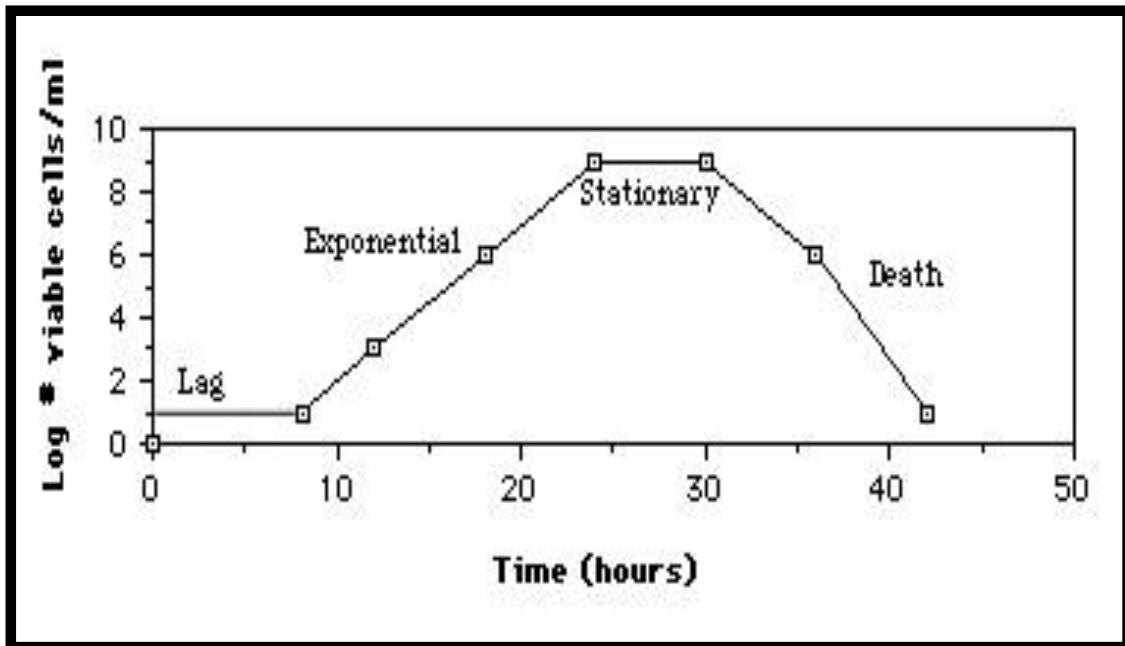
The **bacterial growth curve** represents the number of live cells in a bacterial population over a period of time.

Generation time: The time required for a population of cells to double in number.

*The **bacterial growth curve** passes through 4 distinct stages or phases:

1- Lag Phase: This initial phase is characterized by cellular activity but not growth. A small group of [cells](#) are placed in a nutrient rich medium that allows them to synthesize [proteins](#) and other molecules necessary for replication. These cells increase in size, but no [cell division](#) occurs in the phase.

2- Exponential (Log) Phase: After the lag phase, bacterial cells enter the exponential or log phase. This is the time when the cells are dividing by binary fission and doubling in numbers after each generation time. Metabolic activity is high as [DNA](#), [RNA](#), [cell wall](#) components, and other substances necessary for growth are generated for division. It is in this growth phase that [antibiotics](#) and disinfectants are most effective as these substances typically target bacteria cell walls or the protein synthesis processes of [DNA transcription](#) and [RNA translation](#).



3-Stationary Phase: Eventually, the population growth experienced in the log phase begins to decline as the available nutrients become depleted and waste products start to accumulate. Bacterial cell growth reaches a plateau, or stationary phase, where the number of dividing cells equal the number of dying cells. This results in no overall population growth. Under the less favorable conditions, competition for nutrients increases and the cells become less metabolically active. [Spore](#) forming bacteria produce endospores in this phase and [pathogenic bacteria](#) begin to generate substances (virulence factors) that help them survive harsh conditions and consequently cause disease.

4-Death Phase: As nutrients become less available and waste products increase, the number of dying cells continues to rise. In the death phase, the number of living cells decreases exponentially and population growth experiences a sharp decline. As dying cells lyse or break open, they spill their contents into the environment making these nutrients available to other bacteria. This helps spore producing bacteria to survive long enough for spore production. Spores are able to support life.

Enterobacteriaceae

General character:

They are G-ve rods, All motile with peritrichate flagella except *Shigella* and *Klebsiella*, non-spore forming, non-acid fast, All ferment sugar with or without formation of gas Inoculation on MacConkey's or Eosin-Methylene Blue (EMB) agar differentiates family members by lactose fermenting ability, All reduce nitrates into nitrites form, catalase positive, All are oxidase negative, facultative anaerobes, normal part of the gut flora found in the intestines of humans and other animals, while others are found in water or soil, example for Enterobacteriaceae is *Escherichia*, *Salmonella*, *Shigella*, *Klebsiella*, *Proteus*, *Enterobacter*, *Yersinia*, etc.

Virulence and Antigenic Factors of Enterobacteriaceae

- Ability to colonize, adhere, produce various toxins and invade tissues
- Some possess plasmids that may mediate resistance to antibiotics
- Many enterics possess antigens that can be used to identify groups
- O antigen – somatic, heat-stable antigen located in the cell wall
- H antigen – flagellar, heat labile antigen
- K antigen – capsular, heat-labile antigen K antigen is called the **Vi** (virulence) antigen in *Salmonella typhi*.

Taxonomy of *Enterobacteriaceae*:

- Differentiation is based on biochemical reactions and differences in antigenic structure
- Over 30 genera and 120 species
- More than 95% of clinically significant strains fall into 10 genera and less than 25 species

Clinical Manifestations

A. Some members of the *Enterobacteriaceae* are **true pathogens**

- *Salmonella* spp.
- *Shigella* spp.
- *Yersinia* spp.
- Certain strains of *Escherichia coli*

B. Most members of the *Enterobacteriaceae* are **opportunistic** or cause secondary infections of wounds, the urinary and respiratory tracts, and the circulatory system

Types of Infectious Disease

- **Intestinal (diarrheal) infection**

- **Extra intestinal infection**

Urinary tract infection (primarily cystitis and prostatitis and pyelonephritis)

Respiratory (nosocomial pneumonia)

Wound (surgical wound infection)

Bloodstream (gram-negative bacteremia)

Central nervous system (neonatal meningitis)

Spontaneous bacterial peritonitis (Usually in patients with liver ailments)

Endocarditis (Vascular endocardia surface inflammation)

Escherichia coli

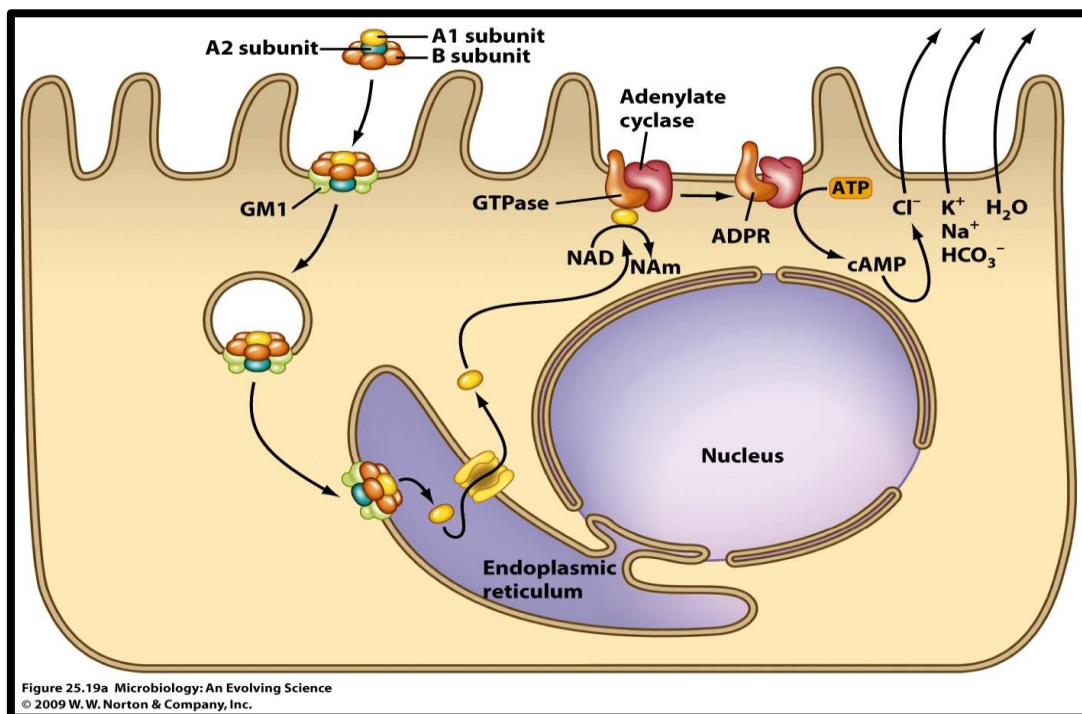
It lives in human or animal intestine. Detection of *E. coli* in drinking water is taken as evidence of recent pollution with human or animal excreta. Wide range of infection including meningitis, , urinary tract, wound, bacteremia and **Gastrointestinal Infections include:**

- **Enteropathogenic (EPEC)** – Diarrhea with large amounts of mucous without blood or pus occurs along with vomiting, malaise and low grade fever.
- **Enterotoxigenic (ETEC)** – “traveler’s diarrhea”; watery diarrhea without blood
- **Enteroinvasive (EIEC)** – produce dysentery with bowel penetration types produce disease resembling shigellosis in adults and children
- **Enterohemorrhagic (EHEC) serotype 0157:H7 they have Shiga-like toxins and also called STEC (shigella toxin E.coli)** – associated with hemorrhagic diarrhea and hemolytic-uremic syndrome (HUS)
- **Enteroadgregative (EaggEC)** – cause diarrhea by adhering to the mucosal surface of the intestine; watery diarrhea

Biochemical reaction:

It ferments lactose, glucose, sucrose, maltose and mannitol with acid and gas. Indol and methyl red is positive (v-p) and citrate is negative. Urease is not hydrolysed. H₂S is not produce.

- **Virulence factors**
- **Toxins**
- **Enterotoxins** – produced by enterotoxigenic strains of *E. coli* (ETEC). Causes a movement of water and ions from the tissues to the bowel resulting in **watery diarrhea and other infection**. There are two types of enterotoxin:
 - **LT – is heat labile** LT is composed of two types of subunits. One type of subunit (the B subunit) binds the toxin to the target cells via a specific receptor that has been identified as Gm1 ganglioside. The other type of subunit called (the A subunit) is then activated by cleavage of a peptide bond in reaction.
 - **ST – is heat stable** and binds to specific receptors to stimulate the production of cGMP with the same results as with LT .
 - Both enterotoxins are composed of five beta subunits (for binding) and 1 alpha subunit (has the toxic enzymatic activity).



proteus

General characters:

The *proteus* organisms are G-ve. Motile, aerobic. Most species are free-living in water, soil, sewage and All are normal intestinal flora. Non lactose fermenter, non-capsulated, non-spore forming. Pleomorphic, **It has a characteristic "swarming" pattern** (growth as ring revolved form similar to waves connection from center) and is an opportunistic pathogen of humans. It is known to cause urinary tract infections and wound infections. The species are:

1- *P. vulgaris*

2- *P. mirabilis*

3- *P. rettgeri*

4- *P. morganii*

Clinical samples:

1- Urine

2- Stool

3- Sputum

4- Pus

Biochemical test

Proteus species do not usually non ferment lactose, but have shown to be capable lactose fermenters depending on the species in a triple sugar iron (TSI) test. It is oxidase-negative, but catalase- and nitrase-positive. Specific tests include urease positive and Only Enterobacteriaceae that makes phenylalanine deaminase tests. Produce powerful **urease**, which rapidly hydrolyzes urea to ammonia and carbon dioxide and the follow show the differentiation between coliform bacilli and proteus:

TABLE 26-4 Differentiation of Coliform Bacilli and *Proteus* Found in Human Clinical Specimens

Organism	Motility	Lactose	Indole	Urease	H ₂ S	Other
<i>Escherichia coli</i>	+	+	+	—	—	
<i>Klebsiella pneumoniae</i>	—	+	—	+	—	large mucoid colonies
<i>K oxytoca</i>	—	+	+	+	—	large mucoid colonies
<i>Enterobacter aerogenes</i>	+	+	—	—	—	some strains mucoid, LD+, AD—
<i>E cloacae</i>	+	+	—	d	—	LD—, AD+
<i>E sakazakii</i>	+	+	[—]	—	—	yellow pigment, LD—, AD+
<i>E gergoviae</i>	+	d	—	+	—	LD+, AD—
<i>Pantoea agglomerans</i>	+	d	[—]	[—]	—	some strains yellow pigment, LD—, AD—
<i>Serratia marcescens</i> ^a	+	—	—	—	—	some strains red pigment
<i>S rubideae</i> ^b	+	+	—	—	—	red pigment
<i>Citrobacter freundii</i>	+	d	—	d	+	
<i>C koseri</i> ^c	+	d	+	d	—	
<i>Proteus mirabilis</i>	+	—	—	+	+	"swarming" motility
<i>P vulgaris</i>	+	—	+	+	+	"swarming" motility

+ (≥ 90% strains positive), d (26-75% strains positive), [—] (11-25% strains positive), — (0-10% strains positive)
LD (lysine decarboxylase), AD (arginine dihydrolase)

^a *S liquefaciens* group and *S ficaria* have same five reactions shown.

^b *S fonticola*, *S odorifera*, and *S plymuthica* have same five reactions shown.

^c *C amaloneticus* and other *Citrobacter* have same five reactions shown.

Pathogenesis and Virulence

Adherence factors

- **Fimbriae**- facilitate adherence and thus enhance the capacity of the organism to produce disease
- *Proteus* bacilli possess **somatic O and flagellar H antigens**

Symptoms

The first sign that you have a *Proteus mirabilis* urinary tract infection will often be in your urine. You may notice that your urine is suddenly coming out darker or smellier than before. In some cases, you will even see blood in your urine. Another sign of a urinary tract infection is the increased urge

to urinate, even if little or no urine comes out. You should also not be surprised if you feel a burning sensation when you do urinate. It is common with most types of urinary tract infections, Blood comes out of the boils and a feeling of burning and pain accompanied by itching occurs in the skin injuries that the physical therapist works to treat.

Pathogenicity:

- 1- UTI
- 2- Pyogenic lesions like abscess, infection of wound, ear, and respiratory tract bedsores.

Treatments

Known antibiotics that *proteus* is sensitive to:

Ciprofloxacin

Ceftazidime

Netilmicin

Sulbactam or Cefoperazo

Meropenem

Piperacillin /tazobactam

Antibiotics should be introduced in much higher doses than "normal" when *proteus* has infected the sinus or respiratory tissues.

Staphylococcus

- 3 -

General Characters:

- 1- They are G +, Ovoid or spheroidal, Non motile arranged in groups usually form irregular clusters the cluster formation is due to cell division occurring in three planes with daughter cell tend to remains in close proximity , facultative anaerobic.
- 2- On the culture media they form colonies and produced pigment White, yellow or golden yellow in color their hemolytic capacity is variable.
- 3- They are catalase positive, oxidase negative, ferment glucose, and have teichoic acid in their cell walls.

Classification:

A- On the basis of pigment production 3 types of staphylococci are identified.

- 1- *Staphylococcus aureus* produce golden yellow colonies and are pathogenic.
- 2- *Staphylococcus albus* produce white colonies and are nonpathogenic.
- 3- *Staphylococcus citreus* produce lemon-yellow colonies and are nonpathogenic.

B- On the pathogenicity based on the synthesis of the **Coagulase-positive** strains:

- 1- Pathogenic species Coagulase-positive strains like *Staphylococcus aureus* (CPS)
- 2- Non pathogen species Coagulase-Negative strains like *Staphylococcus epidermides* (CNS).

C- Presence of hemolysis. While others don't have any hemolysis, *Staphylococcus aureus* has Beta hemolysis.

There are at least three Staphylococci species of clinical importance:

1. *Staphylococcus aureus* is the most pathogenic for humans.
2. *Staphylococcus epidermidis*, which is part of the normal flora and is of low pathogenicity grown on the skin.
3. *Staphylococcus saprophyticus* which can cause urinary tract infections.

Some Biochemical test for Staphylococcus

The type of test	<i>Staphylococcus aureus</i>	<i>Staphylococcus albus</i>	<i>Staphylococcus citreus</i>
Catalase test	+	+	+
Coagulase test	+	-	-
Hemolysis test	Beta on (Blood agar)	None	None
Color differences in colonies on Mannitol salt agar	Gold – yellow	White	lemon to yellow

Staphylococcus aureus

Biochemical reaction:-

They ferment number of sugar production acid and no gas (glucose , lactose , sucrose , maltose , mannitol) .

Culture characterization:

Nutrient agar

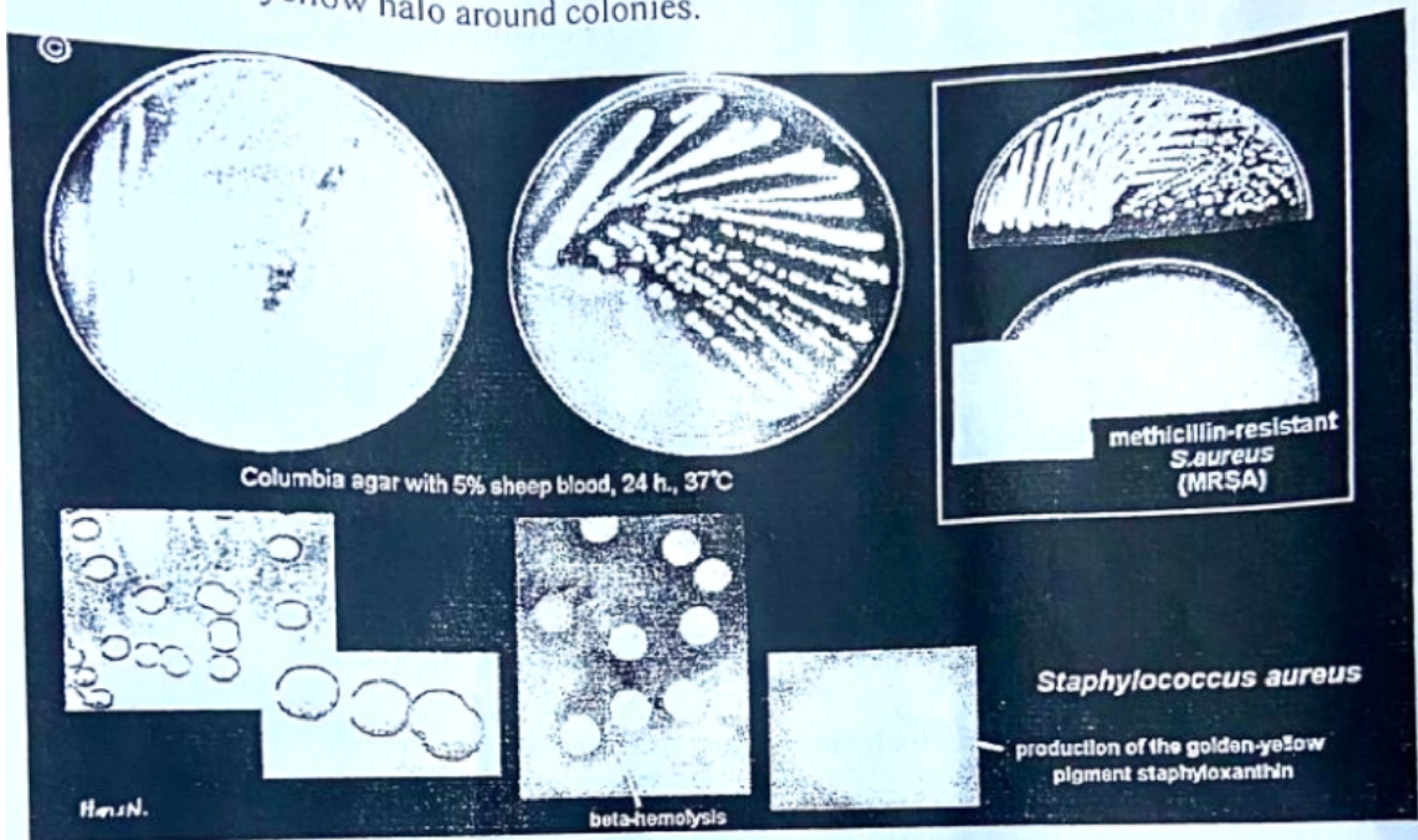
After incubation colonies are pigmented golden yellow (size from 2-4 mm) circular, convex, opaque with entire edge, pigment production enhanced when 1 % glycerol mono acetate or milk is incorporated in medium.

Blood agar:

A wide zone of β - haemolysis (clear zone) is produced around colonies.

Egg yolk medium: the organism produce Shiny, black colonies surrounded by an inner opaque (lipase reaction) halo and clearing zones (protease reaction)

Mannitol salt agar: the media contain 7- 10 % NaCl, Yellow colonies; may have yellow halo around colonies.



Toxins

1. Toxic epidermal is caused blistering skin lesions in neonates and young
2. Toxic shock syndrome toxin (TSST) The toxin causes a range of symptoms including fever, diarrhea, TSST can be fatal. and can also be caused by *Streptococcus pyogenes*.
3. Haemolysin: *Staph. aureus* produces at least 3 types of haemolysin known as Alfa, beta and gamma. Beta haemolysin haemolysis rabbit and sheep red cell rapidly.
4. Leucocidin: Leucociden is closely associated with delta lysis damage polymorphonuclear leucocyte.
5. Enterotoxin: The toxin is responsible for infection of Staph. food poisoning, vomiting an diarrhea within 6 hours of taking contaminated food.

Various enzymes and protein produced by staphylococci

Product	Physiological action
B-lactamase	Breaks down penicillin
Catalase	Converts hydrogen peroxide into water
Coagulase	Binds complex structure called staphylothrombin in which a clot is formed
DNase	Destroys DNA
Lipase	Break down Lipid molecules
Protease	Break down proteins

Clinical Infection

Staphylococci can cause many forms of infection include:

- A. **Cutaneous lesions:** Pustules are common in acne,
- B. **Deep infection:** Acute osteomyelitis, tonsillitis, pharyngitis, sinusitis, pneumonia, pulmonary abscess.
- C. **Staphylococcal food poisoning:** It is results when food contaminated with enterotoxin produced by Staphylococci is consumed e.g. meat, fish, milk and milk products. Diarrhea and vomiting set in within 6 hours of taking contaminated food.

Treatment

The antibiotic of choice for the treatment of *S. aureus* infection is Cloxacillin, or Erythromycin if the patient is allergic to penicillin. and Methicillin-resistant many strains of *S. aureus* (MRSA) or used vancomycin .